

Atty Dkt. No.: CLON-035CIP
USSN: 10/006,922

REMARKS

Formal Matters

This response is supplemental to Applicants' Amendment and Response filed on September 27, 2005. Applicants respectfully request entry of all amendments made in the September 27, 2005 response. Applicants present herein additional arguments with respect to the outstanding rejections under 35 U.S.C. § 112, first paragraph, and respond to the outstanding rejection under 35 U.S.C. § 112, second paragraph. Applicants' arguments advanced in the September 27, 2005 are incorporated by reference in their entirety in this supplemental response.

Minor amendments to the claims have been made. Claims 14 and 15 have been cancelled. Claims 22 and 27 now recite *selected from the nucleic acids according to Claim 1*. The latter changes are ones of style. Support may be found in original claims 22 and 27.

Personal Interview

The Examiner and her supervisor are thanked for the personal interview with Applicants' representative Richard A. Schwartz on January 4, 2006. During the interview, the article by Shaner et al. Nature Biotechnology, published online November 21, 2004; doi:10.1038/nbt1037 was discussed. Applicants had faxed a copy prior to the interview to the Examiner on January 3, 2006. In addition, Applicants' representative presented the Examiner with two sequence alignment charts, which show that fluorescent proteins of Shaner et al. have at least 80% sequence identity with Applicants' SEQ ID NO:12. Applicants' representative pointed out that post-filing date publications may be used to substantiate statements in Applicants' application as filed, and cited *In re Hogan*, 194 USPQ 527, 537 (CCPA 1977).

This account is believed to be a complete and accurate summary of the interview as required by 37 C.F.R. § 1.133. If the Examiner believes that this summary is inaccurate or incomplete, Applicants respectfully request that the Examiner point out

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any deficiencies in her next communication so that Applicants can amend or supplement the interview summary.

Rejections Under 35 U.S.C. §112, second paragraph

Claims 6, 7, 14-23, and 27 have been rejected under 35 U.S.C. § 112, second paragraph. This rejection is respectfully traversed. The claims have been rejected for the following reasons:

The Examiner asserted that claim 6 is indefinite by virtue of the recitation of the phrase *substantially the same*. Present claim 6 does not recite that phrase. This rejection may be withdrawn.

The Examiner asserted that claims 6, 7, 16, 18, and 20 are indefinite by virtue of the recitation of the phrase *at least 10 residues in length*. Claim 16 has been cancelled, and present claims 6, 7, 18, and 20 do not recite that phrase. This rejection may be withdrawn.

The Examiner asserted that claims 14 and 15 are indefinite for reasons that are now moot by virtue of the cancellation of these claims. This rejection may be withdrawn.

The Examiner asserted that claim 16 is indefinite by virtue of the recitation of the phrase *a fragment of a nucleic acid*. Claim 16 has been cancelled. This rejection may be withdrawn.

The Examiner asserted that claim 18 is indefinite by virtue of the recitation of the phrases *hybridizes under stringent conditions, its complementary sequence, and substantially the same*. Present claim 18 does not recite those phrases. This rejection may be withdrawn.

The Examiner asserted that claims 22 and 27 are indefinite by virtue of the fact that the phrase *selected from the group consisting of* is not followed by a Markush group. Present claims 22 and 27 recite that a nucleic acid (claim 22) or transgene (claim 27) is selected from the nucleic acids of claim 1. This rejection may be withdrawn.

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Rejection Under 35 U.S.C. §112, first paragraph (Scope of Enablement)

Claims 1-23, 27, and 31-47 have been rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to provide enablement "for any fragment, mutant or mimetic [of the nucleic acid of SEQ ID NO: 11] ... or a transgenic organism or progeny thereof." July 6, 2005 Office Action at page 8. This rejection is respectfully traversed. In view of the amendments to the claims and the arguments advanced by Applicants in their previous response, as well as the following additional arguments, this rejection may be withdrawn.

In the Examiner's Interview Summary dated September 13, 2005, the Examiner asserted that "percent language such as '70%' in [previously presented] Claim 1 would be problematic" under both the enablement and written description requirements of § 112, first paragraph. Applicants respond as follows:

Applicants attach hereto an article by Shaner et al. *Nature Biotechnology*, published online November 21, 2004; doi:10.1038/nbt1037 m (Exhibit A), as well as amino acid alignments of the fluorescent proteins disclosed by Shaner et al. compared to Applicants' SEQ ID NO:12. The alignments show clearly that the Shaner et al. proteins have at least 80% identity with SEQ ID NO:12 (Exhibit B). Therefore, these mutants should be considered as working examples of the invention as presently claimed.

In addition, Shaner et al. validates statements made in Applicants' specification as of Applicants' filing date. Accordingly, the data of Shaner et al. are tantamount to additional working examples, despite the fact that Shaner et al. was published after Applicants' filing date. It is well established decisional law that all available evidence of enablement of an application as of its filing date must be considered, whenever that evidence becomes available, including after the filing date. *In re Hogan*, 194 USPQ 527, 537 (CCPA 1977).

When rejecting a claim under the enablement requirement of section 112, the Examiner bears the "initial burden of setting forth a reasonable explanation as to why [she] believes that the scope of protection provided by [the] claim is not adequately enabled by the description of the invention provided in the specification." *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The Examiner bears

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the burden of providing evidence or technical reasoning to substantiate her doubts that the specification is not enabling with respect to the scope of a claim sought to be patented. *Ibid.* See also MPEP § 2164.04. Without evidence or technical reasoning to doubt the truth of the statements made in the application, the application must be considered enabling. *Ibid.* In addition, an enablement rejection should be stated with a full development of the reasons rather than by a mere conclusion coupled with some stereotyped expression. MPEP § 706.03.

Furthermore, the Examiner is reminded that without evidence or technical reasoning to doubt the truth of the statements made in the application, the application must be considered enabling. Applicants do not bear the burden of proving statements made in their application. Nevertheless, Applicants have now put forth evidence and working examples to show that the full scope of their claimed invention is enabled.

The Examiner's mere doubting or gainsaying of Applicants' statements is not evidence or technical reasoning. The proper applicable evidentiary standard for determining enablement is a preponderance of the evidence standard, i.e., a *more likely than not* or greater than a 50% chance standard. Therefore, mere unsubstantiated doubting of enablement, without providing sufficient documentary evidence, does not satisfy this standard because mere doubting results in a 50-50 tie, and does not evince that the Examiner is *more likely than not* correct. As such, a tie is broken in favor of Applicants.

Rejection Under 35 U.S.C. §112, first paragraph (Written Description)

Claims 1-23, 27, and 31-47 have been rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking written description for the claimed genus of nucleic acid fragments and mutants. July 6, 2005 Office Action at page 6. This rejection is respectfully traversed. In view of the amendments to the claims and the arguments advanced by Applicants in their previous response, as well as the following additional arguments, this rejection may be withdrawn.

However, in the Examiner's Interview Summary dated September 13, 2005, the Examiner asserted that "percent language such as '70%' in [previously presented]

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Claim 1 would be problematic" under both the enablement and written description requirements of § 112, first paragraph. Applicants respond as follows:

The Examiner is reminded that "[c]ompliance with the written description requirement is essentially a fact-based inquiry that will 'necessarily vary depending on the nature of the invention claimed.' *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 65 USPQ2d 1385 (Fed. Cir. 2003)(quoting *Enzo Biochem v. Gen-Probe, Inc.*, 296 F.3d 1316, 1324, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002). Furthermore, the written description requirement "law ... will vary with differences in the state of the knowledge in the field and differences in the predictability of the science." *Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005). The Office must analyze and make of record "what one skilled in the art would have understood from the ... disclosure or the degree of predictability of technical variations in this field of art. *Bilstad v. Wakalopulos*, 386 F.3d 1116, 1126, 72 USPQ2d 1785 (Fed. Cir. 2004).

Applicants submit that there is sufficient written description for one with knowledge and skill in this particular art to recognize that Applicants were in possession of their generic invention without the need for an exhaustive disclosure of additional representative embodiments. Furthermore, the Shaner et al. paper published after Applicants' filing date, not only validates statements made in Applicants' statements, but also in so doing shows predictability in this art. Therefore, Applicants have satisfied the written description requirement.

Finally, Applicants submit that because Applicants' disclosure is enabling for the full scope of their claims (see arguments advanced *supra*), the written description requirement is *ipso facto* satisfied as well. The court has held that the "two requirements [enablement and written description] usually rise and fall together. That is, a recitation of how to make and use the invention across the full breadth of the claim is ordinarily sufficient to demonstrate that the inventor possesses the full scope of the invention, and vice versa." *Lizardtech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1345 (Fed. Cir. 2005).

In view of the above, it is submitted that the claims do comply with the written description requirement. The specification provides multiple representative examples,

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including working examples of representative nucleic acids encoding exemplary variant proteins, such that one of skill in the art would have no doubt that the applicant was in possession of the *invention* as claimed at the time the application was filed.

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CONCLUSION

In view of the above remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issuance. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone Bret Field at 650 327 3400.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815.

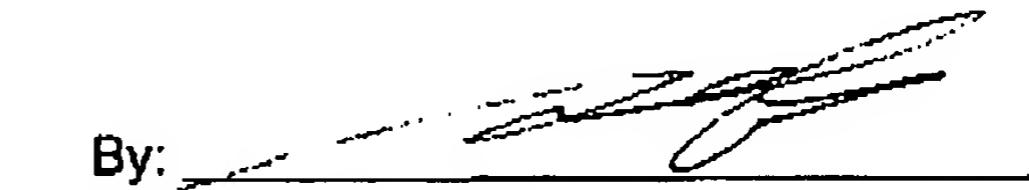
Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: January 13, 2006

By: 

Richard A. Schwartz
Registration No. 48,105

Date: January 13, 2006

By: 

Bret E. Field
Registration No. 37,620

Enclosures:

- **Exhibit A** - Shaner et al. Nature Biotechnology, published online November 21, 2004; doi:10.1038/nbt1037 m.
- **Exhibit B** - Alignments showing that the Shaner et al. proteins have at least 80% identity with SEQ ID NO:12.

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